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October 27, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: 21 CFR Parts 210, 211, 820, 1271
[docket no. 97N-484S]
Suitability determination for donors of...

To Whom It May Concern:

These comments indicate those areas of the proposed rule that would negatively affect infertility therapy.

1. The prohibition from usina non-auarantined ('fresh') oocytes to produce preanancv. This prohibition will radically alter the practice of assisted reproduction in this area, at great cost to patients and without apparent benefit:
   a. Only about 70% of frozen embryos survive, and even those that do are less potent in producing pregnancy. Thus, prohibiting fresh embryo transfers would lose a large proportion of the current pregnancy potential. In order to restore the same overall chance for success as currently exists, patients will clearly have to do more treatment cycles. What is the projected cost to the patient of this regulatory change?
   b. Even if cryopresetvation could be improved such that it had no negative effect on pregnancy potential, it would still add to the cost of the effort (typically about $2000 to freeze and $2000 to thaw). Have these costs been analyzed?
   c. Requiring quarantining of all embryos delays the opportunity to conceive by at least 6 months. This delay is decidedly unwelcome to couples anxious to have a family, and will in and of itself increase the risk of obstetric complications (which rise inexorably with age). Have these risks been considered?

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d. Cryopresetvation adds risk to the procedure:
   i. Are you sure that cryopreservation is entirely safe? Might it not damage DNA or other vital cellular structures and lead to more birth defects? To argue that no such evidence exists is to beg the question: what evidence do you have that infectious diseases risks are real that these? (I'm unaware of any evidence that infections can be passed on to patients through the oocyte).
   ii. What if no embryos survive? Who pays for the wholesale loss of this chance for pregnancy? Has this cost been included in your models?
   iii. What if the oocyte donor isn't available for retesting, or has a change of heart and withdraws her consent for the use of her eggs? Who pays for the cost of having screened her, stimulated her to make eggs, retrieved them, fertilized them, and then stored these embryos? Have these outcomes (and their costs) been considered in your analysis?

e. Are there any reported cases of harm that have come to patients via donor oocytes, and if so, would they have been avoided by the quarantining and retesting of the donor which you propose? Have the estimated levels of infectious risk that stem from the current practice of transferring fresh embryos been considered, and how high a risk would need to exist before regulations such as these were adopted?

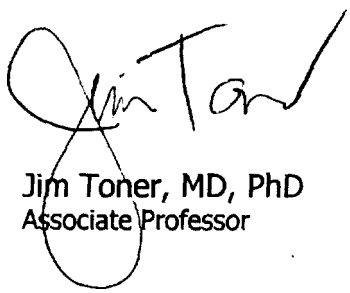
2. What to do with positive screening tests. If a donor tests or screens positive for a 'relevant communicable disease' (e.g., HBV, HBC, CMV, Chlamydia, Gonorrhea, etc.), under what conditions can she be used as a donor? For instance,
   i. If the disease can be eradicated by antibiotics (e.g., Chlamydia), can she then be used?
   ii. If the disease also exists in the intended host but cannot be eradicated (e.g., CMV), can she be used as a donor?
   iii. If the donor has HBV or HBC and the recipient does not, can she be used as an oocyte donor (since there is no evidence that these viruses can live in eggs)?

3. Analysis of Economic Impacts. This section of the notice entirely ignores the economic consequence of prohibiting the use of fresh donor eggs on the increased costs (in money and time), which patients and/or their payers must bear. Since cryopreservation in and of itself adds extra cost, and lowers the chance for pregnancy, patients will experience dramatic reductions in pregnancy rates. Thus, in order to achieve the goal of pregnancy, you would be requiring patients to "pay more to get less": they will on average have to try more times and thus spend more money to get access to the same pregnancy rates they now enjoy.

While safety is an important consideration, and is the one you are charged to assess, you have focused on infectious disease risks to the exclusion of all others. What about the risk of embryo damage from freezing? It is perhaps as likely a source of risk as the one you focus on, and would be increased by your proposal. Perhaps the risks are thus offsetting. One thing we can be sure of is that your proposed regulations will lead to higher costs (in both time and money). And while I applaud your focus on risk, to what extent are these risks

real, or are they phantoms? This needs to be addressed. I believe that in the absence of strong evidence of probable risk, that fresh embryo transfers be permitted with appropriate patient consent (as now occurs).

Sincerely yours,



Jim Toner, MD, PhD
Associate Professor

cc: American Society of Reproductive Medicine
Society for Assisted Reproductive Technologies
Senator Ron Wyden

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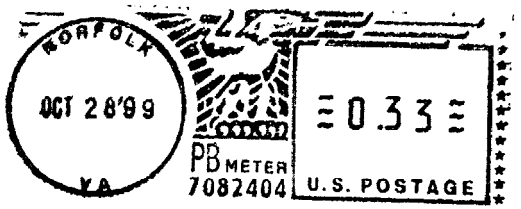

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